Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
01 SEP 2015	**N/A**	**-**

4. TITLE AND SUBTITLE	5a. CONTRACT NUMBER
Complexity and animal models	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)	5d. PROJECT NUMBER
Batchinsky A. I.,	5e. TASK NUMBER
	5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)	8. PERFORMING ORGANIZATION REPORT NUMBER
United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release, distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a REPORT	b ABSTRACT	c THIS PAGE			
unclassified	**unclassified**	**unclassified**	**UU**	**1**	

Variability and work

Peter T. Macklem

An essential feature of life is adaptability combined with stability. Ordered open thermodynamic systems, for example, crystals, are stable but not adaptable. Chaotic systems, for example, weather, are adaptable but unstable. Both adaptability and stability are found in complex systems at the phase transition between order and chaos. This combination leads to continuous variation of physiologic parameters. Where a system is situated between ordered and chaotic systems depends on the amount of energy that the system imports from the environment. If so, one might predict that the magnitude of variations would increase with metabolic rate. For muscle, however, the ability to adapt depends on the work the muscle is already doing (W) relative to the maximum work it can perform (Wmax). The greater W/Wmax is, the less adaptable the muscle is to new demands. Thus, anything increasing W or decreasing Wmax will decrease adaptability and possibly also variability. Seely (personal communication) has measured heart and respiratory rate variability during incremental exercise. Both decreased as exercise increased. Thus, the relationship between variability and W/Wmax in health might quantify resting W/Wmax for the heart and respiratory muscles by measuring resting heart and respiratory rate variability. A variation of this hypothesis occurs in asthma where the magnitude of variation of impedance to airflow in the lung is increased. But it is likely that airway smooth muscle is unloaded in asthma; and this would decrease W/Wmax, thereby maintaining the relationship between variability and W/Wmax.

doi:10.1016/j.jcrc.2010.05.012

Complexity and animal models

Andriy I. Batchinsky

Noninvasive monitoring and distant assessment of status of the injured may revolutionize critical care if data analysis techniques can be validated that identify physiologic deterioration before changes in conventional vital signs.

For the last several decades, monitoring and diagnosing injury severity have been based on changes in time averaged means of heart rate and blood pressure interpreted in context of visual assessment of the patient. However, changes in heart rate and blood pressure generally do not occur until compensatory mechanisms are exhausted. The latter may explain why conventional vital signs are poor and late descriptors of life threatening changes in the patients' condition. A recent study reported that 23% of prehospital trauma patients with normal vital signs required life saving interventions. To make matters worse, visual assessment of the patient may not be possible during mass casualty and natural disaster situations or may need to be postponed during combat to avoid danger to the medic's life. To improve our ability to monitor and diagnose critical illness in the civilian setting and to assess combat casualties from a distance, we need new vital signs that are superior to conventional vital signs in their ability to provide timely assessment of injury severity and predict the need for life saving interventions.

The 2 presentations by Dr Batchinsky provide an insight into the research pertinent to the development of new vital signs carried out within the US Army Institute of Surgical Research Combat Critical Care Engineering Task Area.

The first presentation, "Complexity in Animal Models," is an overview of recently completed and ongoing research at the US Army Institute of Surgical Research involving various animal models of hemorrhagic shock, resuscitation, trauma, inhalation injury, apnea, and other critical states. This research serves as a test bed for discovery, development, and validation of new vital signs before they are introduced to human critical care. We feature a project under development that involves comprehensive continuous analysis of real life electrocardiograms designed to detect changes in patients during various critical states using methods from heart rate variability and heart rate complexity analysis. A special focus is on demonstrating limitations set by signal quality as well as caveats and limitations of many of the explored methods as applicable to analysis of nonstationary data and data containing ectopic beats collected during ventricular fibrillation and cardiopulmonary resuscitation. The second presentation will be summarized below.

doi:10.1016/j.jcrc.2010.05.013

Neural dynamics and networks

Andre Longtin

This talk will review our past work on the method of surrogate data analysis. We will discuss the conditions under which it can be applied to time series data, as well as point process (event) data. We will also discuss this work in the context of biomedical applications and discuss how well it has been suited to building models of the physiologic processes. Finally, we will present our approach to modeling physiologic systems with stochastic delay differential equations.

doi:10.1016/j.jcrc.2010.05.014

Heart rate variability and the autonomic nervous system

Gwynne Jones

The autonomic nervous system (ANS) with its parasympathetic and sympathetic nervous systems (SNS) and its multiple forebrain, midbrain, and medullary interconnecting nuclei would certainly qualify as a complex system. Merely the efferent arm of the SNS with catecholamine output to 9 receptors (3 β, 3 α 1, and 3 α 2) would alone suggest something rather complex. Stimulation of their efferent second messengers (adenyl cyclase and guanadyl cyclase) to generate cyclic adenosine monophosphate and cyclic guanosine monophosphate is further modulated by ±14 phosphodiesterases. In addition, the phosphodiesterases are positioned in strategic intracellular positions to further refine the effect of the cyclic adenosine monophosphate and cyclic guanosine monophosphate. Thus, merely the SNS motor output is exquisitely refined to modulate this complex nonlinear process.

Afferent traffic informing the ANS central nuclei adds further mind numbing complexity. This is affected by a multiplicity of local sensors using a host of physical and chemical mediators. These include interoceptors for the milieu interieur (pain, ischemia, oxygen sensors, CO_2 sensors, oxygen radicals, adenosine,